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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,225	07/13/2007	Daichang Yang	023231-00033	9090
4372	7590	11/21/2008	EXAMINER	
ARENT FOX LLP			WORLEY, CATHY KINGDON	
1050 CONNECTICUT AVENUE, N.W.				
SUITE 400			ART UNIT	PAPER NUMBER
WASHINGTON, DC 20036			1638	
			NOTIFICATION DATE	DELIVERY MODE
			11/21/2008	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DCIPDocket@arentfox.com  
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<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/584,225	YANG ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	CATHY K. WORLEY	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 03 June 2008.  
 2a) This action is FINAL.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-13 is/are pending in the application.  
 4a) Of the above claim(s) 12 and 13 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-11 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____ .
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date <u>6/23/06; 6/23/08</u> .	6) <input type="checkbox"/> Other: _____ .

## DETAILED ACTION

### ***Restriction/Election***

1. In response to the communication received on June 3, 2008, from Dawn C. Russell, the election with traverse of group I, claim 10 (in part) as it relates to the wheat puroindoline b promoter, is acknowledged. Claims 1-9 and 11 are linking claims, and therefore they are also included in this election. The Applicant argues that there is no burden on the Patent Office to examine the groups of claims together (see second paragraph of response). This is not persuasive, however, because the restriction was based on lack of unity rather than being based on a showing of burden. Furthermore, there is an additional burden to search for two additional promoters; such as the promoters of Groups II and III (the PDI and HSP70 promoters, respectively); and there is an additional burden to search for methods wherein protein is accumulated in at least two different intracellular regions, as in Groups IV and V. For these reasons, the restriction requirement is proper and is **MADE FINAL**. The Applicant is reminded to amend claim 10 to read only on the elected promoter, the wheat puroindoline b promoter.

Claims 1-13 are pending in the instant application. Claims 12 and 13 are withdrawn because they are directed to non-elected inventions. Claims 1-9, 11, and 10 (in part) are examined in this Office Action.

***Claim Objections***

2. Claims 1, 2, and 10 are objected to for the reasons below:

- Claim 1 is objected to because of the following informalities: in step (a) the claim utilizes a plant cell from a monocot plant that has not, yet been grown (the plant is grown in part (b)). This appears to be an oversight of claim construction; and the Applicant is advised to amend part (a) to replace “a plant cell of the monocot plant” with - - a monocot plant cell - - .
- Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The Examiner is not aware of any monocot seed-specific signal peptides that are not N-terminal signal peptides; therefore, this limitation does not further limit claim 1. If the Applicant is aware of a non-N-terminal signal peptide that is monocot seed-specific, then please bring this to the attention of the Examiner and this objection will be withdrawn.
- Claim 10 is objected to because of the following informalities: there is a typographical error; Applicant is advised to replace “purindoline” with - - puroindoline - - . In addition, the Applicant is reminded to amend claim 10 to delete the recitations of the non-elected promoters.

Appropriate correction is requested.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-4, 10, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Digeon et al (PMB (1999) Vol. 39; pp. 1101-1112).

The claims are directed to a method of producing seeds of a monocot plant that accumulate a heterologous protein; wherein the method utilizes a promoter from a monocot non seed storage protein gene and a signal peptide.

Digeon et al teach the production of rice seeds that express glucuronidase (GUS) under the control of the wheat puroindoline-b promoter, including the expression of translational fusions that comprise the N-terminus of the purindoline-b protein (see pages 1105-1106). Digeon et al teach the promoter from the wheat puroindoline b gene (see Figure 1). They teach that puroindoline proteins are synthesized as preproteins with N-terminal and C-terminal propeptides (see first paragraph on page 1101). They teach expression of a heterologous protein (GUS) as a translational fusion that comprises the first 39 bp of the puroindoline coding sequence, which presumably encodes the N-terminal signal sequence which directs the protein to the endoplasmic reticulum and the secretory pathway (see Figure 2). They teach seeds produced by the transgenic rice plants (see right

column on page 1106), and they teach that GUS was assayed by a fluorometric GUS assay, which inherently means that the seeds were processed to produce a fraction comprising the GUS protein and the GUS was extracted from the seeds. Because claim 11 does not contain any limitations regarding the percent purity of the protein, extracting the GUS protein to be able to perform the fluorometric GUS assay is sufficient to meet the limitations in this claim.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 5-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitelam, G.C. (J. Sci. Food Agric. (1995) Vol. 68; pp. 1-9) in view of Digeon et al (PMB (1999) Vol. 39; pp. 1101-1112).

The claims are directed to a method of producing seeds of a monocot plant that accumulate a heterologous protein; wherein the method utilizes a promoter from a monocot non seed-storage protein gene and a signal peptide; and wherein the protein is an animal protein, a mammalian protein, a human protein, and/or a protein from a selected list of proteins.

The instant claims are obvious over the prior art because there was some teaching, suggestion, or motivation in the knowledge generally available to one of ordinary skill in the art to combine the reference teachings, and there was a reasonable expectation of success in combining the teachings.

#### **SCOPE AND CONTENT OF THE PRIOR ART – PRIMARY REFERENCE**

Whitelam teaches the production of recombinant proteins in plants (see entire article). They teach that production in seeds is attractive because they are convenient for long-term storage and also because they can be used as an edible delivery system for vaccines or therapeutic agents (see left column on page 8). They teach the production of human serum albumin (HSA), antibodies, and antibody fragments (see page 3), and vaccines and amylase (see page 6), and phytase (see page 7). They teach that HSA protein was directed for secretion via the endoplasmic reticulum and was not produced at detectable levels without a signal or pro-sequence (see left column on page 3). Whitelam teaches that ScFv protein was purified from cultured cells be secretion into the culture medium (see left column on page 6) and they teach that one procedure for purification from bulk seed is to produce the recombinant protein as a fusion with oleosin which targets the fusion to oil bodies and enables easy purification (see right column on page 2).

#### **DIFFERENCES BETWEEN THE CLAIMED INVENTION AND THE TEACHINGS OF WHITELAM**

Whitelam does not teach a monocot plant or a promoter or signal peptide from a monocot non seed-storage protein gene.

#### SCOPE AND CONTENT OF THE PRIOR ART – SECONDARY REFERENCE

Digeon et al teach the promoter from the wheat puroindoline b gene (see entire article). They teach that puroindoline proteins are synthesized as preproteins with N-terminal and C-terminal propeptides (see first paragraph on page 1101). They teach expression of a heterologous protein (GUS) as a translational fusion that comprises the first 39 bp of the puroindoline coding sequence, which presumably encodes the N-terminal signal sequence (see Figure 2).

#### LEVEL OF ORDINARY SKILL IN THE PERTINANT ART

The pertinent art is the field of molecular biology, and one of ordinary skill in this art would have earned a Ph.D. in molecular biology, biochemistry, plant biology, or some other related field. One of ordinary skill in this art would have been well-versed in techniques for heterologous expression of recombinant proteins and would be familiar with the literature encompassing production of therapeutic proteins in plants. This skill level is evidenced by the skill level of Whitelam and the authors whose work is cited by Whitelam in his review article.

#### FINDING OF OBVIOUSNESS

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to combine the teachings of Whitelam and Digeon et al. These teachings include each element recited in the instant

claims. Because Whitelam et al teach that expression in seeds is an attractive design choice, one of ordinary skill in the art would have been motivated to combine the teachings of Digeon et al and Whitelam to arrive at the instant invention.

Digeon et al teach that the wheat puroindoline-b promoter drives expression of a recombinant protein in transgenic rice seeds, therefore, one of ordinary skill in the art would have been motivated to utilize the wheat puroindoline-b promoter. In addition, Whitelam teaches that a signal sequence is important for increasing expression of a recombinant protein in a plant; and therefore, one would have been motivated to utilize the N-terminal signal peptide of the wheat puroindoline-b protein. Given the multiple successes in production of recombinant proteins in plants that are taught by Whitelam and given the success, specifically, of producing a recombinant protein in a transgenic rice seed using the wheat puroindoline-b promoter and signal peptide that was taught by Digeon; one would have had a reasonable expectation of success in combining these teachings. For these reasons, the instant claims are obvious over the prior art.

5. No claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner is on a variable schedule but can normally be

reached on M-F 10:00 - 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Cathy K. Worley/  
Primary Examiner, Art Unit 1638